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Chemical Measures of Similarity Among Disinfection By-Product Mixtures

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There are few measures that can be used to distinguish among mixtures of disinfection by-products (DBPs) produced in the chlorination or chloramination of drinking water. Objective measures of similarities among DBP mixtures would greatly simplify judgments about the risk that may be associated with exposure to DBPs in a given water supply. Major by-products of chlorination/chloramination include the trihalomethanes (THMs) and haloacetic acids (HAAs), which are routinely measured for compliance to regulations. A key question is whether measurement of similar amounts of these DBPs is indicative of the myriad other DBPs that are known to be produced. This article utilized data from a survey of 35 utilities in the United States that included several additional parameters, including members of the haloacetonitrile, trihaloacetaldehyde, and halopropanone classes. Based upon the distribution of bromine in the THM class, the concentrations of unmeasured brominated and bromochlorinated compounds could be determined. This allowed determination of whether measures of the THM and/or HAA classes reflected the amounts of these less abundant classes. Variations in relative yields among DBP classes were observed with water source type and with whether chlorine or chloramine was used as the disinfectant. However, most of the variability was attributable to geographic location. The relative abundance of brominated by-products also varied among water sources. Recent documentation that potent by-products, such as nitrosamines, are selectively produced in particular water systems and preferentially with chloramination indicates that more measures of individual DBP are needed to evaluate similarity among DBPs mixtures.

The mixture of chemicals that is created when chorine is added to drinking water is very complex. It is probable that several hundreds or even thousands of compounds are produced in the treated water (Krasner et al., 2006). The adverse health consequences from exposure to these disinfection by-products (DBPs) depend upon the individual and collective toxicological properties of each of these compounds.

To evaluate health risks of complex mixtures such as DBPs, risk assessors employ either component-based or whole-mixture methods. This series of articles focuses on whole-mixture methods. When using whole-mixture methods, a risk analyst determines whether the toxicity of the mixture of concern (i.e., the mixture encountered in the environment) is "sufficiently similar" to that of the tested mixture. If the mixtures are similar, then dose-response data from the tested mixture can be used to evaluate the health risk posed by the mixture of concern. Thus, determining whether the toxicity of the mixture of concern is "sufficiently similar" to that of a tested mixture or a group of tested mixtures is central to the use of whole-mixture risk assessment methods (U.S. EPA, 2000; Rice et al., 2008).

Ideally, judgments of similarity among mixtures are based on analytic chemistry and toxicology data for both mixtures. Because comprehensive chemistry and toxicity data are infrequently available for both mixtures, risk assessors typically rely on available chemistry data. For example, mixtures of DBPs that occur in different source waters or at different times of the year in the same source water can be quite variable (Bull et al., 2009). Determining whether mixtures of DBP obtained from different sources or at different times of the year from the same source are similar requires a set of measurable parameters that can be used to identify important differences among DBP mixtures that affect health endpoints or significantly alter the relationship between the DBP exposure and response. Given

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the set of conditions described in Bull et al. (2008) that affect formation of different classes of DBP, a data set was sought that would provide information on production of by-products that extend beyond those that are regulated currently in the United States. Inferences of possible differences in adverse health effects associated with exposures to these DBP mixtures or in DBP dose-response could then be drawn from the analytic differences among these mixtures (see discussion of limitations of DBP health effects data in Bull et al., 2008).

The chemical analyses reported in the 35-utility study sponsored by the U.S. Environmental Protection Agency (U.S. EPA) and the Association of Metropolitan Water Districts (U.S. EPA, 1989) was used to determine the extent to which mixtures of DBP might vary from site to site and within a utility over time. This database was selected because it (1) was of modest size, (2) examined waters from diverse sources, (3) included documentation of treatment processes used, (4) measured a set of non-regulated by-products, (5) included data that would aid in understanding the chemistry of a particular water supply (i.e., total organic carbon [TOC] measurements, bromide concentrations, pH, and temperature), and (6) analyzed a sample for each season of the year from each system.

There were two other candidate studies that evaluated DBP levels at multiple sites that were not included in this analysis, a multi-utility study reported by Krasner et al. (2006) and the DBP data collected under the U.S. EPA Information Collection Rule (Obolenksy & Singer, 2005). Although Krasner et al. (2006) measured a number of less abundant DBPs, their study was conducted at a smaller number of utilities than the U.S. EPA (1989) study. The small number of utilities examined precluded an assessment of statistical validity of relationships between the less abundant DBPs and those that are more commonly measured.

This article also does not examine data reported from the Information Collection Rule study because it did not analyze the less abundant DBPs (Obolenksy & Singer, 2005). At the time of preparation of this article, all of the data from the Information Collection Rule study had not been reported; thus, these data could be the subject of a future sufficient similarity analysis for DBP mixtures.

Because there are a limited number of variables that can be examined with a sampling of 35 utilities, this article is limited to evaluating those systems that used chlorine or chloramine as the means of disinfecting water. Within this limited context, the article also attempts to address systematic variations in mixtures of DBPs that appear to be related to different sources of water (i.e., groundwater [GW] vs. surface water) and disinfection strategies (chloramine vs. chlorine). While the 35-utility study provides a great deal of useful data to evaluate similarity of chemical composition of DBP mixtures, to more completely evaluate similarity, an approach was sought to estimate the amounts of halogenated by-products within a DBP class based on the incomplete measures that were mandated by United States regulations at the time of the study.

The first step was to develop estimates of the amounts of halogenated by-products within some of the less abundant DBP classes based on the incomplete measures reported in U.S. EPA (1989). This was accomplished by developing a method for estimating the concentrations for brominated and bromochloro members of the class that had not been measured. The relative degree of bromine to chlorine substitutions is estimated by examining the distribution of such substitution within the trihalomethane (THM) class. The degree of bromine substitution is influenced primarily by the amount of bromide that is in the treated water, although it is also modified by the amount of organic carbon that is present relative to the bromide content (Krasner et al., 1996; Obolensky & Singer, 2005). The yield of DBP classes per unit of TOC in the treated water was used to examine inherent variability of precursor quality within and among water supplies. A subsequent article (Feder et al., 2008) utilizes the chemical parameters developed in this article to assess the utility of statistical methods for evaluating the similarity of DBP mixtures based on differences in chemical composition.

METHODOLOGY

A major difficulty in assessing variability in DBPs in drinking water supplies is that nonregulated DBPs are infrequently measured. Measures of the regulated THMs (chloroform, bromodichloromethane, dibromochloromethane, and bromoform) and selected members of the haloacetic acid classes (haloacetic acid 5 [HAA5], which includes monochloroacetic acid, monobromoacetic acid, dichloroacetic acid [DCA], dibromoacetic acid [DBA], and trichloroacetic acid [TCA]) are now available for most drinking-water supplies, and more data will be available in the future because of the unregulated contaminants monitoring program (U.S. EPA, 2007). The 35-utility study provides information on five additional DBP classes, the haloacetonitriles, trihalopropanones (THPs) by measurement of 1,1,1-trichloropropanone (TCP), dihalopropanones (1, 1-DHPs) by measurement of 1,1-dichloropropanone (DCP), halopicrins by measurement of chloropicrin, and one trihaloacetaldehyde (THALD) by measurement of trichloroacetaldehyde, also known as chloral hydrate (CH). The availability of this additional information permits some expansion of the conventionally measured DBP to evaluate the potential complexity of DBP mixtures.

The analysis focused on three parameters that were developed to allow a more dependable characterization of variability in byproducts in disinfected water. These parameters are (1) measures of individual by-products, (2) total yields of DBP classes, and (3) the specific yield of DBP. To account for missing members of DBP classes, this study developed an approach for estimating the yields associated with the last two parameters.

The method for expanding these classes considered the probable amounts of brominated by-products that were not measured in many of the classes of halogenated by-products (Table 1). Developing an estimate of the by-product class concentrations depends on a number of assumptions. The

TABLE 1
Illustration of the Predictions Made in This Article of the Concentrations of Unmeasured Halogenated By-Products and Total Class Yields in a Given Water Supply

	No chlorine	Monochloro	Dichloro	Trichloro
Single halogen	Bromoacetic acid	Chloroacetic acid		
	Bromoacetaldehyde	*Chloroacetaldehyde*		
	Bromoacetonitrile	*Chloroacetonitrile*		
	1-Bromopropanone	*1-Chloropropanone*		
	3-Bromopropenal	*3-Chloropropenal*		
	Cyanogen bromide	*Cyanogen chloride*		
Double halogen	Dibromoacetic acid	**Bromochloroacetic acid**	Dichloroacetic acid	
	Dibromoacetaldehyde	*Bromochloroacetaldehyde*	*Dichloroacetaldehyde*	
	Dibromoacetonitrile	Bromochloroacetonitrile	Dichloroacetonitrile	
	1,1-Dibromopropanone	**1-Bromo-1-chloroproanone**	1,1-Dichloropropanone	
	3,3-Dibromopropenal	*3-Bromo-3-chloropropenal*	*3,3-Dichloropropenal*	
Triple halogen	Bromoform	Dibromochloromethane	Bromodichloromethane	Chloroform
	Tribromoacetic acid	**Dibromochloroacetic acid**	**Bromodichloroacetic acid**	Trichloroacetic acid
	Tribromoacetaldehyde	**Dibromoacetaldehyde**	**Bromodichloroacetaldehyde**	Chloral hydrate
	Tribromoacetonitrile	**Dibromochloroacetonitrile**	**Bromodichloroacetonitrile**	Trichloroacetonitrile
	1,1,1-Tribromopropanone	**1,1-Dibromo-1-chloropropanone**	**1-Bromo-1,1-dichloropropanone**	1,1,1-Trichloropropanone
	Bromopicrin	**Dibromochloropicrin**	**Bromodichloropicrin**	Chloropicrin
Substituted on multiple carbons	*2,2,3-Tribromopropenal*	*2,2-Dibromo-3-chloropropenal*	*2-Bromo-2,3-chloropropenal*	*2,2,3-Trichloropropenal*
	2,3-Dibromopropenal	*2-Bromo-3-chloropropenal*	*2,3-Dichloro-3-bromopropenal*	
		2-Chloro-3-bromopropenal		
	3-Bromo-4-(dibromomethyl)-5-hydroxy-2(5H)-furanone	*3-Bromo-4-(bromochloromethyl)-5-hydroxy-2(5H)-furanone*	*3-Bromo-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone*	*3-Chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone*

Note. Prediction of missing members was done by interpolation or extrapolation. Note that these predictions are based upon the measurement of at least one DBP in a class and the degree of bromination in a completely characterized class, such as the THMs or DHANs. Underlined by-products are those for which measurements were made in the 35-utility study. Those printed in bold are those whose concentrations were predicted. Italicized by-products are examples of compounds whose presence should be strongly suspected. The latter group is not exhaustive of all possibilities.

first is that the relative amounts of bromine and chlorine in by-products of different classes were equivalent. Because the reaction rates of bromine are always more rapid than chlorine, this is probably a reasonable assumption (Amy et al., 1994, 1998). Two other assumptions are more speculative. One is that different substrates react in the same way and the other is that all by-products within a class have roughly the same stability under the conditions occurring in the treated water. Productions of different DBP classes occur at different rates (Reckhow & Singer, 1985), and several classes of DBP are known to be unstable depending upon water conditions. The specific assumption in this project was that within-class stabilities are similar. This is more reasonable than the broader assumption; however, it is likely that certain fully brominated forms of some classes (e.g. tribromoacetic acid) are less stable than their fully chlorinated analogs for steric reasons. Overall, it is unlikely that these errors would invalidate the use of this approximation for identifying differences in precursor quality. Subsequent studies will examine these assumptions in more detail, but require much better characterization of by-product formation rates than are available in the current literature.

The ratios available from the THM and dihaloacetonitrile (DHAN) classes have been used to estimate relative molar yields of trihalogenated, dihalogenated, and monohalogenated by-products within the trihaloacetic acid, dihaloacetic acid, trihaloacetaldehyde, trichloropropanone, dichloropropanone, and chloropicrin classes. These figures were summed and divided by the TOC concentration in the finished water (expressed as mg/L) to estimate the relative amount of a halogenated by-product class that was produced in a given water supply when measurements have been limited to those compounds that were regulated.

The following group of test questions was addressed as a validation of this approach utilizing the data that were available within the 35-utility study:

1. Can the degree of halogenation between by-products within one class be reliably used to gauge the halogenation within another class with a similar degree of substitution?
2. Are there consistent relationships between the formation of one group of DBPs and another (or one individual by-product and another with similar degrees of halogen substitution in another class)?
3. Are there disparities based upon the degree of halogenation (i.e., between mono-, di-, or trihalogenation on the same carbon atom)?
4. Discrepancies in question 1 may arise by differential stability of a DBP. Are discrepancies attributable to differential stability as influenced by another water parameter, such as pH?

RESULTS

Validation of Interpolations and Extrapolations

The validity of two operations performed on the data was tested within the data provided. It was assumed that the relative levels of brominated and chlorinated by-products would be consistent across by-product classes. This was directly tested by determining whether the bromine to chlorine (Br/Cl) ratios found in the THM class correlate with the Br/Cl ratio of the DHAN class. Figure 1 is a plot of the relationship and displays a near linear relationship with a correlation coefficient of $r = .968$.

Second, the validity of using interpolation to calculate the relative degree of bromination within DBP classes was tested in different classes by comparing the relative amounts of dichloroacetonitrile (DCAN), bromochloroacetonitrile (BCAN), and dibromoacetonitrile (DBAN) to project the concentrations of bromochloroacetic acid (BCA) from concentrations of DCA. This was tested by determining whether the DBAN and DCAN ratios were consistent with the DBA/DCA ratios observed (data not shown). The degree of bromination between the two pairs of by-products was closely correlated ($r = .946$). This justified the use of the relative amount of BCAN to DCAN and DBAN to estimate the concentration of BCA.

Based upon these two tests of the hypothesis, it was concluded that the formation of additional members of mixed bromochloro and strictly brominated by-products within a class could be used to reconstruct a probable composition of the entire class.

Comparison of DBP Yields in Different Water Systems

Figure 2 depicts the relative distribution of bromine and chlorine within the THM measured in the 35-utility study (U.S. EPA, 1989). Eighteen of the systems utilized chlorine and 14 used chloramine for disinfection. To avoid bias, systems using ozone or chlorine dioxide for disinfection were excluded from this analysis. The Br/Cl ratios in the THMs varied by

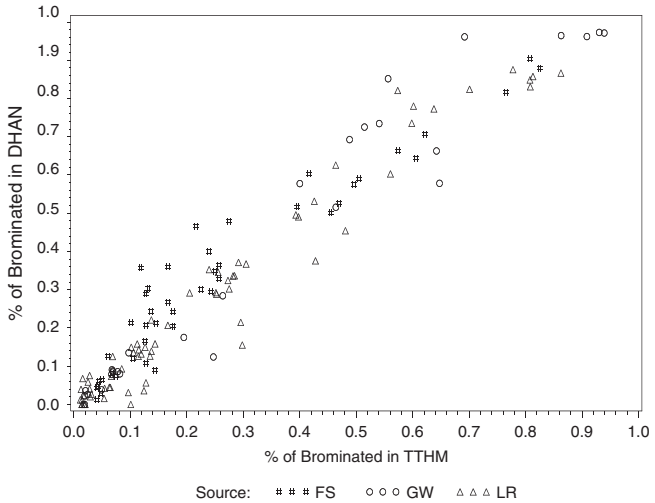

FIG. 1. The relationship of total halogen as bromine in DHANs versus the percentage of total halogen in TTHMs in the U.S. EPA 35-utility study. Water source types are indicated as FS, flowing stream; GW, groundwater; and LR, lake or reservoir.

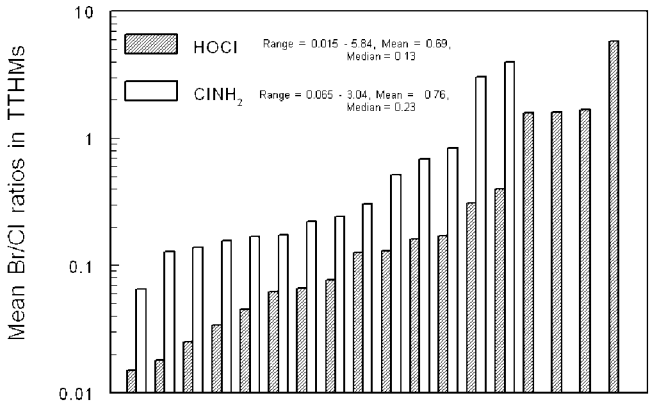

FIG. 2. Distribution of Br/Cl ratios in THMs in chlorinated versus chloraminated drinking water. Data are derived from 32 of 35 water systems in the U.S. EPA (1989) study.

almost 3 orders of magnitude among the 32 systems. A systematically higher Br/Cl ratio was observed in chloramine-treated water versus chlorinated water.

Table 2 illustrates that the yield of DBP classes varies widely among water systems. First, the range of yields of different DBP classes per unit of TOC concentrations was found to differ by factors in excess of 100. This variability is not simply an artifact of the projection of total yields in each by-product class because the variation of the classes where all members were measured was similar. Total trihalomethane (TTHM) yield per milligram TOC varied by a factor of 185 and the yield of the DHAN by 21. There are several variables in the database that potentially contribute to the variability of by-product yield. Two are explored in some detail: the water source type and whether chlorine or chloramine was used as the primary disinfectant.

There were significant differences in all by-product yields depending upon the source water type (Table 3). Disinfected water obtained from flowing streams (FS) yielded the highest overall yields of halogenated by-products per milligram TOC. However, the differences in yields of less frequently measured DBP classes, such as 1,1-dihalopropanone (1,1-DHP), were not large. For the common DBP classes, lake and reservoir (LR) water generally had the second highest yields. However, this pattern was not maintained in some of the less frequently measured classes such as monohaloacetates (MHA), (1,1-DHPs). Judging by the size of the standard deviations of the means, LR water was found to be more variable in TTHM and TTHA classes among systems than FS waters were. Despite this pattern of variability with the two major classes, 1,1,1-THPs were clearly more variable in FS water. The THALD class was by far the most variable class. A note of caution is needed here because the higher degree of variability for this DBP class in GW systems appeared to arise in those systems having high Br/Cl ratios and might be partially artifactual (discussed more fully later). The production of total DHAN per milligram TOC per liter was similar between GW and water from LR, but reduced by about 30% relative to water from FS. Organic carbon from GW yielded less of the 1,1,1-THP class than was observed from the chlorinated surface water sources.

In Table 4, the amounts of each DBP class that was produced per milligram TOC in chlorinated versus chloraminated systems are compared. The only by-product class that was

TABLE 2
Yields of Disinfection By-Product Classes per Unit of Treated Water Total Organic Carbon (TOC)

By-product class	Minimum	Maximum	Mean	SD
THM	1.92[a]	355	109	77
THA	0	186	32	31
DHA	0	120	41	24
MHA	0	33	4.9	4.8
THAN	0	0.48	0.03	0.09
DHAN	4.4	92	34	20
1,1,1-THP	0.015	39	5.3	5.2
1,1-DHP	0.16	15	3.1	2.2
THALD	0	223	21	30
Halopicrins	0	5.5	0.90	1.03

[a]Yield expressed as nmol total by-product class/mg TOC/L in the treated water.

THM, trihalomethanes; THA, trihaloacetic acids; DHA, dihaloacetic acids; MHA, monohaloacetic acids; THAN, trihaloacetonitriles; DHAN, dihaloacetonitriles; 1,1,1-THP, 1,1,1-trihalopropanones; 1,1-DHP, 1,1-dihalopropanones; THALD, trihaloacetaldehydes.

TABLE 3
Yield of Disinfection By-Product Classes per Milligram Total Organic Carbon (TOC) per Liter in Treated Water from Different Sources

By-product class	Ground water	Flowing stream	Lake and reservoir
Total THM[a]	101 ± 100	143 ± 66	90 ± 86
Total THA[a]	19 ± 32	47 ± 38	27 ± 20
Total DHA[a]	29 ± 23	57 ± 26	35 ± 18
Total MHA[a]	5.1 ± 4.6	6.5 ± 6.6	3.5 ± 3.6
Total DHAN[a]	30 ± 22	43 ± 19	31 ± 18
Total 1,1,1-THP	3.6 ± 4.5	6.5 ± 9.0	5.1 ± 3.9
Total 1,1-DHP[a]	3.2 ± 3.2	3.7 ± 2.2	2.7 ± 1.5
Total THALD	11 ± 32	32 ± 36	18 ± 21
Total halopicrins[a]	0.25 ± 0.35	1.3 ± 1.1	0.88 ± 1.01

Note. Yields expressed in nmol total by-product class/mg TOC ± SD by ANOVA and pairwise comparison. THM, trihalomethane; THA, trihaloacetic acids; DHA, dihaloacetic acids; MHA, monohaloacetic acids; DHAN, dihaloacetonitriles; 1,1,1-THP, 1,1,1-trihalopropanones; 1,1-DHP, 1,1-dihalopropanones; THALD, trihaloacetaldehydes.

[a]Significant difference by source at $p < .01$.

TABLE 4
Yield of Disinfection By-Product Classes per Milligram Total Organic Carbon (TOC) per Liter in Water Treated by Chlorine Versus Chloramine

By-product class	Free chlorine (n = 18)	Chloramine (n = 14)
Total THM	115 ± 74	108 ± 78
Total THA[a]	28 ± 23	41 ± 41
Total DHA	43 ± 24	42 ± 27
Total MHA	4.6 ± 5.4	5.4 ± 4.2
Total DHAN	38 ± 19	32 ± 21
Total 1,1,1-THP	5.8 ± 4.3	5.1 ± 6.7
Total 1,1-DHP	3.1 ± 2.3	2.9 ± 2.0
Total THALD	20 ± 28	23 ± 36
Total halopicrins	0.9 ± 0.9	0.8 ± 0.8

Note. Yields expressed in nmol total by-product class/mg TOC ± SD by ANOVA and pairwise comparison. THM, trihalomethane; THA, trihaloacetic acids; DHA, dihaloacetic acids; MHA, monohaloacetic acids; DHAN, dihaloacetonitriles; 1,1,1-THP, 1,1,1-trihalopropanones; 1,1-DHP, 1,1-dihalopropanones; THALD, trihaloacetaldehydes.
[a]Significant difference by source at $p < .01$.

found to consistently vary between chlorinated and chloraminated systems was the THAs, which were found to be higher than in chlorinated supplies. One of the main reasons for utilizing chloramine is to decrease the formation of THMs, but while the mean levels found in chloraminated systems were lower, the difference across all systems was not statistically significant.

Relative Degrees of By-Product Bromination

The variation in the degree to which by-products are brominated in different water supplies was compared using the bromine to chlorine ratio in the THM class (Table 5). The degree of bromination does not appear to be normally distributed, which is reflected in the differences in most of the mean and median values. The differences among water source types are large primarily because of the highest Br/Cl ratio found in some GW. With the exception of GW, it can be seen that the Br/Cl ratio in LR and FS waters treated with chloramine was greater than in those treated with free chlorine. However, there is a high degree of variability within each source type, and the variability is not solely attributed to source type or treatment.

The extreme Br/Cl ratio in GW is not surprising and is due to the bromide concentrations in source water from mixing with saltwater. The mixing can be introduced by tidal action in rivers and estuaries near the ocean or intrusion into the GW. However, it can also be the result of entrapment of salt water in the ground during geologic evolution. There were only 6 supplies that had Br/Cl ratios above 1. Of these, two were in coastal areas known to be affected by saltwater intrusion. The remainder of the group came from GW in the Great Plains region of the United States. GW in the latter area is known to be affected by underground pockets of saltwater. There were three additional systems that had Br/Cl ratios that varied in the range of 0.3–1.1. All three of these water supplies were in coastal regions where saltwater intrusion is a factor. While the more highly affected systems were GW supplies, other GW supplies had among the lowest Br/Cl ratios.

TABLE 5
Variations in the Degree of Bromination Within the Trihalomethane (THM) Class

Source water	Statistic	Chlorinated	Chloraminated
Ground	Mean	2.13 (n = 4)	0.70 (n = 2)
	Median	1.57	0.71
	Range	0.63–7.7	0.05–0.83
Lake and reservoir	Mean	0.24 (n = 9)	0.91 (n = 7)
	Median	0.069	0.34
	Range	0.012–3.5	0.087–5.3
Flowing stream	Mean	0.30 (n = 5)	0.76 (n = 5)
	Median	0.14	0.28
	Range	0.042–3.3	0.10–4.0

Note. Values expressed as the molar equivalent of bromine to chlorine found in the members of the THM class.

It is of interest to note that the median and mean Br/Cl ratios were both higher in chloraminated than in chlorinated systems. This probably reflects the fact that bromamine formation is not as favored as chloramine formation at pH levels commonly found in drinking water (Issac et al., 1985). Therefore, reactions of bromine with natural organic matter (NOM) will proceed preferentially to those of chlorine in the presence of ammonia.

While the Br/Cl ratios tend to be lower in surface waters, the ranges are quite large (i.e., 40- to 300-fold), indicating that this parameter is a major differentiator among DBP mixtures from differing locations. Therefore, the degree of bromination is a criterion of similarity that can be applied across water supplies.

Correlations Among By-Product Classes

Table 6 provides correlation coefficients for the formation of the different by-product classes that were measured in the 35-utility study. Table 6 displays the slope of the relationship (i.e., an estimate of the relative yield of two sets of by-products). The table separates chlorinated systems from chloraminated systems and distinguishes among the water source types investigated. If the organic precursors are of a consistent character among water systems, the yield of each by-product class should parallel one another. This tests the validity of utilizing one or two by-products as reliable predictors of the occurrence of other by-products that are in the mixture. As the THMs and HAAs are the most commonly measured classes, the correlates focused on whether there was a consistent relationship between

TABLE 6
Correlation in Concentrations of Chlorinated By-Products by Treatment and Source

Base DBP	Correlate	All Cl_2 (n = 18)	Cl_2 GW (n = 4)	Cl_2 LR (n = 9)	Cl_2 FS (n = 5)	All $ClNH_2$ (n = 14)	$ClNH_2$ LR (n = 7)	$ClNH_2$ FS (n = 5)
Chloroform	TCA	0.73	1.0	0.59	0.75	0.91	0.98	0.83
	TCA + CH	0.82	0.99	0.74	0.86	0.92	0.99	0.93
	DCA	0.83	0.99	0.60	0.92	0.87	0.85	0.90
	DCAN	0.77	0.99	0.54	0.72	0.72	0.96	0.31
	CP	0.67				0.31		
	1,1,1-TCP	0.33	0.98	0.42	0.33	0.58	0.92	0.16
	1,1-DCP	0.23	0.78	0.056	0.31	0.35	0.57	0.12
TCA+CH	1,1,1-TCP	0.69	0.99	0.77	0.66	0.80	0.94	0.0071
	1,1-DCP	0.49	0.79	0.056	0.31	0.44	0.57	0.025
DCA	1,1,1-TCP	0.60	0.99	0.83	0.54	0.50	0.71	0.073
	1,1-DCP	0.60	0.83	0.67	0.57	0.46	0.69	0.048

Note. All Cl_2 is inclusive of all chlorinated supplies, and all $ClNH_2$ of all chloraminated systems. There were only two GW that were chloraminated, so this category was omitted from the table. DBP, disinfection by-product; GW, groundwater; LR, lake and reservoir water; FS, flowing streams; TCA, trichloroacetic acid; CH, chloral hydrate; DCA, dichloroacetic acid; DCAN, dichloroacetonitrile; CP, chloropicrin; 1,1,1-TCP, 1,1,1-trichloropropanone; 1,1-DCP, 1,1-dichloropropanone.

these by-products and by-products that were less frequently measured.

The influence of source water on the nature of the DBP mixture is illustrated by the inconsistent relationships among DBPs across water source type. Correlation coefficients among chloroform, TCA, and DCA were certainly significant across all water types. However, some of these were less than 0.6, indicating that they are not entirely predictive of one another. Greater discrepancies are observed in the relationship between the major DBP classes and 1,1,1-TCP and 1,1-DCP. In certain water types there was essentially no relationship at all. For example, 1,1-DCP simply did not correlate with chloroform or TCA + CH in chlorinated LR water, although there is a good correlation in chlorinated GW (because of the limited number of GW systems, this latter correlation may not be as strong as it seems). While 1,1-DCP displays a small correlation with chloroform in chloraminated LR water, there is essentially no correlation in between chloroform and 1,1-DCP in chloraminated FS. On the other hand, positive correlations were obtained between 1,1-DCP or 1,1,1-TCP and DCA in all water source types and in both chloraminated and chlorinated systems, even though some of these were as low as 0.5. There was no significant correlation between 1,1,1-TCP and any of the major DBP in chloraminated FS.

The slopes provided in Table 7 can be taken as indications of the average amounts of the correlated DBPs to the base DBP that were formed under different conditions of treatment and water source type. 1,1,1-TCP yield ranged from nondetectable to as high as 0.052 times that of chloroform across systems, from nondetectable to 0.093 relative to TCA, and from nondetectable to 0.14 relative to DCA. These relatively high yields were all observed in chlorinated GW. In other waters, the yield of 1,1,1-TCP to relative to TCA was consistently higher than the yield relative to chloroform. Similar variation was observed with 1,1-DCP with respect to chloroform and TCA, but the relative yield of 1,1-DCP to DCA fell into a narrow range across all water source types and treatments except chloraminated FS. Thus, the ratios among chlorination DBPs are not consistent across water systems or treatment with chlorine or chloramine.

Variation Within Water Systems

The variability found within water supplies during the year sampled in the 35-utility study was much larger than anticipated. Some seasonal and temperature-dependent differences in yields were expected. However, variation by as much as two orders of magnitude was seen in the relative yields of certain DBP classes per unit of TOC in some systems. Contrary to expectations, this variability was observed in GW as well as surface water.

In general, the THM class was less variable within utilities than other by-product classes. Their concentration varied by ≥3-fold in only 9 of the 35 systems. The smaller variability in this class may reflect closer attention of the utilities to this class of by-products because it was the only one regulated in the late 1980s. However, the variation was observed in systems that did not approach the maximum contaminant level (MCL), indicating that there may be some significant seasonal differences in the precursor characteristics in these systems.

The by-product class that was the most variable was the THALD. The THALD yields were estimated to range from as low as 5 nmol/mg TOC to as high as 160 nmol/mg TOC in one utility (Figure 2), from 10 to 225 in a second, and from 0 to 80 in a third. The extreme shifts have to be viewed with caution

TABLE 7
Slope of Relationship Between Chlorinated By-Products by Treatment and Source

Base DBP	Correlate	All Cl_2	Cl_2 GW	Cl_2 LR	Cl_2 FS	All $ClNH_2$	$ClNH_2$ LR	$ClNH_2$ FS
Chloroform	TCA	0.22	0.30	0.24	0.20	0.32	0.43	0.23
	TCA + CH	0.34	0.36	0.37	0.34	0.49	0.66	0.32
	DCA	0.34	0.38	0.28	0.36	0.48	0.51	0.46
	DCAN	0.066	0.10	0.045	0.042	0.0094	0.16	0.023
	CP	0.0043				0.0055		
	1,1,1-TCP	0.015	0.052	0.025	0.013	0.035	0.074	–0.0035
	1,1-DCP	0.006	0.011	0.0019	0.0019	0.013	0.026	–0.0035
TCA+CH	1,1,1-TCP	0.073	0.15	0.093	0.068	0.091	0.11	0.00045
	1,1-DCP	0.031	0.031	0.026	0.035	0.032	0.040	0.0020
DCA	1,1,1-TCP	0.067	0.14	0.11	0.055	0.055	0.10	–0.0032
	1,1-DCP	0.038	0.031	0.048	0.036	0.032	0.054	0.0026

Note. All Cl_2 is inclusive of all chlorinated supplies, and all $ClNH_2$ of all chloraminated systems. Relative by-product yields (i.e., slopes) are expressed as nmol correlate/nmol of base DBP. DBP, disinfection by-product; GW, groundwater; LR, lake and reservoir water; FS, flowing streams; TCA, trichloroacetic acid; CH, chloral hydrate; DCA, dichloroacetic acid; DCAN, dichloroacetonitrile; CP, chloropicrin; 1,1,1-TCP, 1,1,1-trichloropropanone; 1,1-DCP, 1,1-dichloropropanone.

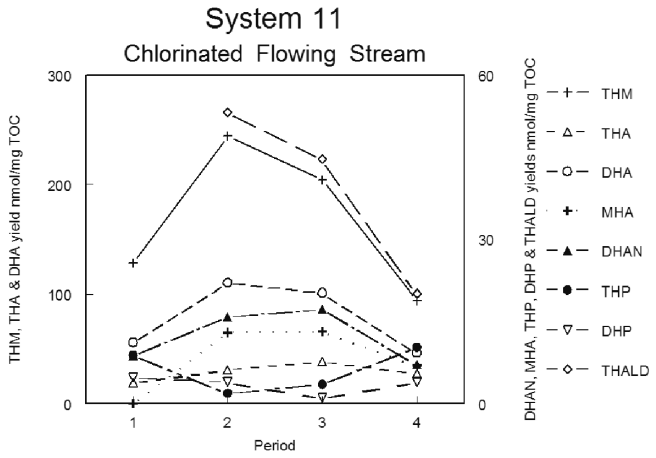

FIG. 3. Variability in the relative yields of disinfection by-product classes per unit of total organic carbon (TOC) during the course of a year in flowing stream water that was chlorinated. Period 1 corresponds to spring, 2 to midsummer, 3 to fall, and 4 to winter. Note that the dihaloacetonitriles, monohaloacetic acid, trihalopropanone, dihalopropanone, and trihaloacetaldehdye classes are graphed to the right axis. The remaining by-products are scaled to the left axis.

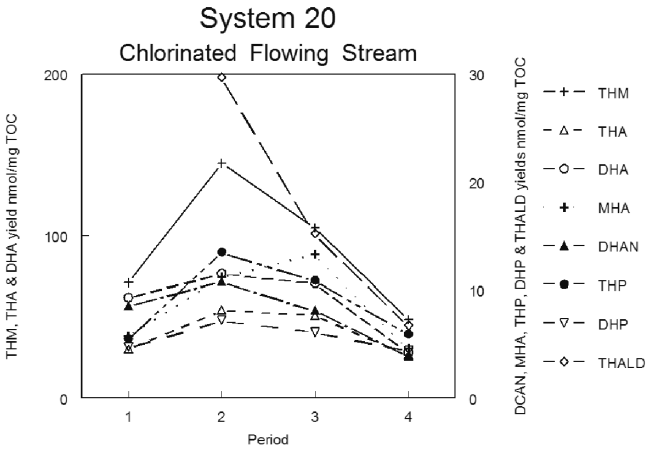

FIG. 4. Variation in the relative yields of different classes of halogenated by-products per unit of total organic carbon (TOC) in a second chlorinated flowing stream water during the course of the year. Period 1 corresponds to spring, 2 to midsummer, 3 to fall, and 4 to winter. Note that the dihaloacetonitrile, monohaloacetic acid, trihalopropanone, dihalopropanone, and trihaloacetaldehyde classes are graphed to the right-hand scale. The remaining by-product classes are graphed to the left-hand scale.

because these were high-bromide waters and the estimate was based on measurement of chloral hydrate, and this fell at or below the detection limits in the other three samples. Such extreme shifts in yields were not found in other systems, but the within-system variability in this class was still >3-fold in 18 of the 35 systems; this was clearly not amplified by the total class calculation.

The pattern in the yield of by-product classes in two chlorinated FS waters illustrates how dissimilar the pattern of by-product yields can be in different systems (Figures 3 and 4). These two utilities are in similar geographic areas, but the total halopropanone yields seen in system 11 is minimal in the second and third period (spring and summer), contrasting sharply with other DBP classes. In contrast, in system 20 all of the DBP appeared to follow the same general pattern by season. The samples were taken on the same days in systems 11 and 20 except for the fall sample, which were taken 2 wk apart. These two systems are on different watersheds but have similar weather patterns and vegetative cover. They are, however, in different regions (Midwest and East Coast), which may

produce some subtle differences in precursor quality at different times of the year.

Figure 3 is a good example of a system where DBP yields varied independently of season. In this case the trihalopropanones decreased markedly during the summer months.1,1-DHP changed to a lesser degree, but with the same downward trend in the summer and fall. However, THM, THALD, DHA, DHAN, and MHA classes were significantly elevated. The THA class was found at similar concentrations at all time periods.

Systematic Differences in By-Product Class Formation with Chlorination and Chloramination

The only by-product class that appeared to be affected consistently by the disinfectant used was THA (Table 4). A statistically significant increase in the mean yield was evident when chloramine was used as the disinfectant as opposed to chlorine. Caution must be used in interpreting these data, as one of the most common uses of chloramine was to suppress the formation of the TTHMs to comply with regulations that were extant in the late 1980s. Systems that chose this method of complying with TTHM regulations would be expected to produce more THMs if chlorine were to be used as the disinfectant. Thus, the relative yields in this report must be interpreted with this fact in mind. Nevertheless, data do show that differential yields of DBP classes occur as a result of substituting the use of chloramine for chlorine as the primary disinfectant.

Chlorinated FS waters were found to display the most intrasystem variability during the course of a year. This distinction was not as clear in chloraminated systems, in that several of the LR systems were quite variable (i.e., systems 4, 7, 10, 25). Of interest is the fact that this variability was not uniformly observed in all the DBP classes, which suggests some variation in the precursor character at different times of the year.

DISCUSSION

Nature of the Problem

DBPs represent a complex mixture to which humans are exposed. The disinfectant reacts with precursor materials in the water to produce a wide variety of by-products (Richardson, 1998; Bull et al., 2001). Chlorine, the most commonly employed chemical disinfectant, both oxidizes and halogenates natural and anthropogenic organic matter. In most drinking-water systems NOM dominates the precursor pool. Other chemical disinfectants, such as ozone, are perceived simply as oxidants, but they also produce halogenated by-products to the extent that they activate bromide present in the treated water. Therefore, various halogenated by-products are found, but there are also various oxidation products that are not halogenated, such as aldehydes, ketones, and organic acids. Another recent study of the occurrence of less frequently measured DBP (Krasner et al., 2006) provides additional variables that could be explored. As that study only included 12 utilities and would require several other DBP classes to be addressed, it was not included in the present study. Despite the limited size of this study, it does provide seasonal data for each of the 12 utilities that could be further pursued to define the extent of within system variability.

As a result of the diverse nature of the toxicology of different classes of DBP, it was important to determine whether their occurrence generally paralleled one another or whether there was some probability that they could vary somewhat independently. This effort was impeded because several members of the DBP classes were not measured in the 35-utility study. Therefore, it was necessary to estimate the levels of these by-products to estimate how much of each class of DBP was produced in each water supply.

A similar approach was used by Obolensky and Singer (2005) to analyze data obtained from the U.S. EPA Information Collection Rule (ICR). These authors identified some variations in the relative incorporation among the DBP classes they analyzed (DHAN > THM > DHAA > THAA), finding mean bromine fraction ratios ranging from 0.79–1.28. Nevertheless, correlation coefficients of the degree of bromination among DBP classes all exceeded 0.86 and were significant. According to their analyses, use of DHAN to predict DHAA concentrations would result in an overestimate of the brominated species in the latter class. Since the 35-utility study included DBA analyses, our predictions were limited to predictions of bromochloroacetic acid by interpolation and are not subject to this error. However, there could be a small bias in prediction of other dihalogenated classes such as 1,1-halopropanones, as only the chlorinated compounds were measured. As indicated elsewhere this prediction was more problematic when measured levels of the fully chlorinated by-product were low and concentrations of bromide were high. Obolensky and Singer (2005) results suggest that precursors of DHAN are more reactive with halogen than the precursors of other dihalogenated DBP classes, consistent with previous findings that precursors react with halogen at differing rates (Reckhow & Singer, 1985).

Evidence of Differences in Precursor Quality by Source

The lack of correlation in yields of certain DBP classes in LR and FS stream water suggests a subtle but systematic difference in a fraction of the precursors for some DBP classes and the precursors for the THM. An influence of precursor quality may be inferred from the wide variation of DCP relative to chloroform formation. The same large difference in yield of DCP in chloraminated versus chloraminated LR water previously noted with DCAN supports the idea that there are some parallels with the chemical character of the precursors for the dichloropropanones and the dihaloacetonitriles. On the other hand, the strikingly different pattern observed with TCP and DCP under these two conditions points to a potentially important difference in precursors involved in the production of these two chemically related by-products.

The consistency seen between TCP and DCP formation with TCA + CH and DCA formation, respectively, also suggests some commonality in the precursors for these two classes. However, the markedly suppressed levels of these two by-products in chloraminated FS water again points to some subtle differences in precursors.

The present article focused on insights that can be gained by examining DBP class yields as an indicator of variations in the quality of organic carbon that contribute to different DBP mixture compositions. It is important to note that variations in treatment can also contribute to differences among DBP mixtures, and this can change between seasons as operators attempt to deal with changing conditions in their source water (Bull et al., 2001). Nevertheless, variations in source water are a major variable that emerged from the analysis of the 35-utility data. LR water quality may be influenced by blooms of microorganisms; FS may reflect both changing runoff patterns and seasonal variations in chemical nature of newly formed carbon on the water shed during the summer and fall months. This variability in the mixture composition in time and space has implications for differences in the type and extent of adverse health effects that might arise from consumption of different mixtures.

Exploring correlations between relative yields of single chlorinated DBPs demonstrates some clear patterns of precursor quality in waters derived from different sources. Further differences may be inferred by comparisons with yields in chloraminated water. If one assumes that there are no systematic differences between waters of similar source types that are chlorinated versus chloraminated, then those reactions suppressed in chloramine disinfected water imply precursors with a lower degree of reactivity. These analyses indicate that no single DBP class is sufficient for concluding that mixtures of DBP from among different water sources are similar.

While there are some systematic variations introduced by water source type and the use of chlorine versus chloramine, most of the variability can simply be attributed to the individual water supply. At least part of this variability has to be due to the differing characteristics of the precursors across geographic regions.

The limited ability to predict the formation of one class of halogenated by-products by the concentrations of another is magnified as extensions are made of the prediction to classes that occur at lower concentrations. If these classes are of limited toxicological potency, this may be of little concern when considering similarity among mixtures. However, this is demonstrably not the case with selected DBPs classes such as the halofuranones and nitrosamines, which are much more potent as mutagens and carcinogens than the THMs or the HAAs. Therefore, when evaluating similarity among mixtures, one must be concerned about the limited toxicological characterization that is available for most DBPs.

The identification of *N*-nitrosodimethylamine (NDMA) as a DBP formed at higher levels in systems that disinfect with chloramine stands as an important example that the occurrence of the important precursors can be independent of the occurrence of bulk precursors included under the rubric of NOM.

Limitations on the Interpretation of the Present Analysis

The 35-utility study represented an important effort to provide a broader indication of DBP formation in U.S. drinking waters than was previously available. However, there are important limitations in the data. Most importantly, this study evaluated a relatively small proportion of DBPs that are produced. While there was representation from the major regions of the United States, data are too sparse to be confident that the few systems surveyed in individual regions to be considered representative of the different water sources within a region. For example, the study did not have sufficient power to accurately characterize the differences in by-product yields of water from different source types (e.g., GW, FS, LR). These were analyzed in the 35-utility data set to determine if some explanations might be found for the variability observed between water supplies. Indeed, the source water type was seen to systematically influence by-product yields, but the major variable remained the individual water system rather than these broad categories of sources. Care must be exercised to avoid inappropriate interpretation of some of the statistical analyses that have been performed with the simple goal of determining the range of differences that might be encountered in various mixtures of DBPs:

1. Suppression of the concentrations of one DBP that occurs as a result of switching from the use of chlorine to chloramine should not be interpreted to mean a reduction of other important DBPs in mixture.
2. Changes in DBP class yield per milligram TOC per liter were primarily used to determine how much the precursor carbon might vary from system to system. This could only be done by expressing the data as nanomoles per milligram TOC. Care must be taken to be certain these are not confused with concentrations of the by-products in a particular water system that are more commonly expressed as micrograms per liter.
3. The expansion of some DBP groups by the addition of the nonmeasured brominated analogs may be appropriate as an indication of the chemistry of formation. While this approximation probably applies to many by-product classes, including some for which no member was measured, it is important to recognize that these projections may contain some errors. For example, heavily brominated compounds may be less stable than their chlorinated analogs. The stability will depend upon the other structural features of the by-product class.
4. In a few cases, the measured concentrations of a by-product were below the limit of detection. This precluded the calculation of the missing members of the by-product class, using this approach. In general, this problem was limited to systems in which there were high levels of brominated compounds in other classes and the detection limit for the

chlorinated analog in the class of interest was too high. Therefore, in these cases one cannot make a valid estimate. That should not be interpreted to mean that members of the class were not present.

5. It should be recognized that the measures investigated here are still quite limited relative to the different types of DBPs that do occur in chlorinated or chloraminated waters. While similarities among systems may be supported by the measures discussed, it is clear that variations in precursors to DBPs that are toxicologically potent might not be reflected in these measures. Thus, additional DBP analyses (i.e., measurement data) and an improved understanding of the individual DBPs and DBP mixture toxicity are needed to increase confidence in judgments that two DBP mixtures are similar. Statistical approaches that use variables identified from these data (Feder et al. 2008) test the null hypothesis that DBP mixtures from different source waters and treatment plants are the same. Confidence in the ability of such methods to distinguish among mixtures is dependent upon the completeness of the available data to fully characterize the mixture.

Parameters from the 35-Utility Study that Illustrate How Judgments Might be Made About the Similarity Among DBP Mixtures

There are a number of parameters that can be used to judge whether mixtures of chlorination by-products obtained from different systems or within the same system using different treatment trains are similar or dissimilar. Some of these are parameters derived from measurements that are routinely made as the result of regulation. Others are measured for purposes of process control (TOC and TOX). Examples of these derived parameters are provided in Table 2. Essentially, these utilize ratios of DBPs to determine how the variables described in this article affect by-product formation in a particular system.

The fraction of the TOX accounted for by measured chlorination by-products will provide some indication of the extent to which the by-product mixture has not been characterized. This parameter was not specifically evaluated in this study. Since TOX has become a much more common measure in drinking water systems, the fraction of the TOX that is uncharacterized in a particular drinking water could be a useful parameter for differentiating among DBP mixtures.

The relative yield of DBP classes provides considerably more information about the nature of byproducts formed in a particular water system than is gained by measurement of all the brominated and mixed bromochloro compounds in a class. As was shown, if one member of the class was measured with some confidence, the remainder of a class could be calculated from the distribution of bromine substitution in the THM class, which is readily measured. The parallel results obtained by Obolensky and Singer (2005) further support this approach. Therefore, a single measurement within each class would allow the calculation of a parameter that would indirectly address the question of what types of precursor predominate in a given water supply. If appropriate kinetic information were to be developed, such a parameter could greatly aid the deficiency of exposure data that has been and continues to be a problem for epidemiological studies of DBPs. The costs of surveys would be minimized because there would be no need to synthesize all the mixed bromochloro standards that are not commercially available.

It follows from this that a measure of the relative amounts of known chloro, bromochloro, and bromo by-products can be reasonably extrapolated to the unknown portion of TOX. Therefore, this provides a measure of the fraction of the TOX that is comprised of brominated by-products. Confidence in this extrapolation reduces the need to measure all members of a given DBP class, as long as one member of each class has been measured and the distribution of bromine to chlorine is known from THM measurements (Obolensky & Singer, 2005).

The dihaloacetate/trihaloacetate ratio can be used to determine whether there are significant differences in the relative yield of dihalo- and trihalo-substituted by-products. This ratio can be related to fundamental differences in precursor character and is detected by the indistinct kinetics of formation (McClellan et al., 2000). The reactivity of these different precursors may be distinctly different with combined chlorine accounting for the greater concentration of dihaloacetates. Such differences have toxicological implications, as the toxicology of the two classes also differs (Bull et al., 2002).

The trihaloacetate/trihalomethane ratio reflects one condition where one can measure decomposition of an intermediate reaction product within the precursor TOC to produce THMs (i.e., the decarboxylation of THAs to form THM under alkaline conditions). This measure will not reflect THM formation from the decomposition of halogenated quinone precursors in NOM that are destabilized by excess free chlorine. In general, decomposition of trihalosubstituted precursors will vary with pH rather than the presence of free chlorine (Bull et al., 2006).

Discovery that NDMA is formed as a result of chlorinating and especially chloraminating drinking water raises the possibility that nitrosamine formation may represent a set of important DBPs not previously recognized. In the presence of appropriate precursors other nitrosamines will be formed in chloraminated water (Mitch & Sedlak, 2002; Charrois et al., 2004). Unfortunately, the occurrence of nitrosable groups in NOM has not been considered (e.g., tryptophan and its microbial metabolites; Bull et al., 2006).

The development of these general parameters should not be viewed as substitutes for measurement of individual DBP once these have been identified as occurring in toxicologically relevant concentrations. Single group parameters, such as the THMs, provided for in drinking-water regulations are not sufficient measures to determine the similarity among DBP mixtures because the components of such mixtures can be seen to vary independently of variation in THMs. This analysis has shown the need

for better identification and toxicological characterization of DBPs that are likely to substantially affect dose-response relationships or alter the nature of expected adverse health effects. Identification of such influential components will provide an improved basis for evaluating similarity among mixtures.

In summary, this analysis of the 35-utility database revealed that the composition of mixtures of DBPs in different locations within the United States was quite variable. Variability in the yield of DBP classes per unit of TOC indicates that there were qualitative differences that probably reflected differences in the quality of precursors from place to place. Other variables within the water treatment plant and distribution system may contribute some of this variability. The important finding was that no single class can serve as an adequate indicator of the mixture of DBPs to which consumers are exposed.

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